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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,397	02/16/2001	Altaf A. Lal	6395-57049	4907

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,397	LAL ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed January 8, 2003. Claims 1, 4-6 and 10 have been amended.

2. Applicant's Declaration under 37 CFR 1.131 (unsigned) and Exhibits A and B filed January 8, 2003 are acknowledged. Applicant's signed Declaration filed February 6, 2003 under 37 CFR 1.131 is acknowledged.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

4. Upon further consideration and review of the instant specification and the prior art it has been determined that claim 10 is not free of the prior art.

Objections Withdrawn

5. a) Objection to claim 6, page 3, paragraph 6 of previous Office action.
b) Objection to claim 10, page 3, paragraph 5 of the previous Office action.

Rejections Maintained

6. The rejection of claims 1,3, 5 and 6 under U.S.C. 102(b) as anticipated by Tine et al is maintained for the reasons set forth on pages 4-5, paragraph 7 of the previous Office action.

The rejection was on the grounds that Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach that the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum* antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). The sequences of the epitopes from each of the life cycles would be inherent in the teachings of the prior art.

Applicant urges that the second Declaration, which reference Exhibits A and B submitted with the first Declaration provides sufficient evidence that the inventors of the current application reduced the invention that is the subject matter of the claims of the current application to practice prior to September 1996, and the effective date of Tine et al. Applicant urges that they have complied with MPEP 715 to overcome Tine et al and request that the rejection of claims 1-3 and 5-6 be withdrawn.

Applicant's arguments filed February 6, 2003 have been fully considered but are not persuasive. The Declaration filed on February 6, 2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Tine et al reference. The Tine et al reference is a statutory bar under 35 U.S.C. 102(b) and thus cannot be overcome by an affidavit or declaration under 37 CFR 1.131. Additionally, it is unclèar as to how the data shown in Exhibits A and B relate to the claimed invention. It is unclear as to what is contained in the clones on for example, page 10 or 12. It is unclear as to what the electrophoresis gels on page 5 represent. It cannot be determined that the data presented in Exhibits A and B is commensurate in scope with the claimed invention.

7. The rejection of claim 1 and 3-6 under U.S.C. 103(a) as being unpatenable over Tine et al et al in view of Schmitt et al is maintained for the reasons set forth on pages 5-7, paragraph 8 of the previous Office action.

The rejection was on the grounds that Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach that the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum* antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column).

Tine et al do not teach the use of a polyhistidine.

Schmitt et al teach affinity purification of histidine-tagged proteins (see the Title). Schmitt et al teach that the expression of recombinant proteins is a standard technique in molecular biology and a wide variety of prokaryotic as well as eukaryotic expression systems are currently in use. Schmitt et al teach that a limiting step is often that the purification of the expressed recombinant protein that yield low expression levels are employed (see the Abstract). Schmitt et al teach that short amino acid sequences can be fused to the recombinant protein as a tag (page 223). Schmitt et al teach that a stretch of 6 histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow a high expression of purified protein (page 229).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the histidine-tag as taught by Schmitt et al to the recombinant poxvirus vectored multiantigen of Tine et al because Tine et al suggest that a NYVAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). It well known in the art to express, characterize and purify recombinant proteins. It is well known in the art to use signal proteins to express recombinant proteins and to use polyhistidine tags to purify recombinant proteins. Schmitt et al teach a stretch of 6 histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow purification of the recombinant protein (page 229). It would have been expected barring evidence to the contrary, that the addition of a His-tag to recombinant proteins would allow for high expression of purified protein. The addition of the His-tag is well within the level of skill in the art.

Applicant urges that a rejection based on Tine et al should not be sustained in view of Applicant's second Declaration filed February 6, 2003, which shows that the inventors of the current application reduced the invention to practice prior to the effective date of Tine et al. Applicant urges that Schmitt et al teach purification of using histidine-tagged recombinant proteins but do not teach a recombinant protein comprising antigenic epitopes of *Plasmodium falciparum* as disclosed in the current application. Applicant urges that Schmitt et al does not render the claims of the current application obvious and Applicant requests that the rejection be withdrawn.

Applicant's arguments filed February 6, 2003 have been fully considered but are not persuasive. The Declaration filed on February 6, 2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Tine et al reference. The Tine et al reference is a statutory bar under 35 U.S.C. 102(b) and thus cannot be overcome by an affidavit or declaration under 37 CFR 1.131.

It is the Examiner's position that Applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al do not teach the use of a polyhistidine. However, Schmitt et al teach affinity purification of histidine-tagged proteins (see the Title). Schmitt et al teach the use of histidine tags to express recombinant proteins. Therefore, it would have been obvious to add the histidine tags of Schmitt et al to the recombinant poxvirus vectored multiantigen of Tine et al because it is well known in the art to express, characterize and purify recombinant proteins using histidine tags. There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 10 is being rejected under 35 U.S.C. 102(b) as being anticipated by Tine et al *(Infection and Immunity, September 1996, p. 3833-3833).*

The claim is drawn to a protein composition comprising the recombinant protein of claim 1, in a pharmaceutically acceptable carrier.

Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach that the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was

demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum* antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). The sequences of the epitopes from each of the life cycles would be inherent in the teachings of the prior art. Tine et al teach the safety and the immunogenicity in nonhuman primates (page 3840, 2nd column). It would be inherent that the recombinant NYVAC-Pf7 vaccine formulations given to nonhuman primates would contain a pharmaceutically acceptable carrier.

Since the Office does not have the facilities for examining and comparing applicant's protein composition with the protein composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein composition of the prior art does not possess the same material structural and functional characteristics of the claimed protein composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

9. No claims are allowed.

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
March 19, 2003

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